

Claims

1. A method for identifying an isolated polypeptide that specifically binds to a neoplastic cell and does not bind to a non-neoplastic cell, said method comprising the steps of (1) providing an isolated cell derived from a healthy
5 donor, (2) isolating a polypeptide produced by the cell, and (3) determining whether said polypeptide specifically binds to a neoplastic cell and does not bind to a non-neoplastic cell.
2. The method of claim 1, wherein said neoplastic cell is not a
10 neuroblastoma cell.
3. The method of claim 1, wherein step (1) further comprises immortalizing said isolated cell.
- 15 4. The method of claim 3, wherein said immortalizing comprises fusing said isolated cell with a myeloma or heteromyeloma cell.
5. The method of claim 1, wherein step (3) comprises determining whether contacting said neoplastic and said non-neoplastic cell with said polypeptide
20 induces apoptosis in said neoplastic cell and not in said non-neoplastic cell.
6. The method of claim 1, wherein step (3) comprises determining whether contacting said neoplastic and said non-neoplastic cell with said polypeptide reduces proliferation of said neoplastic cell and not of said non-neoplastic cell.
25
7. The method of claim 1, wherein said neoplastic cell is a carcinoma.

8. The method of claim 7, wherein said carcinoma is an adenocarcinoma of the colon, diffuse-type stomach carcinoma, adenocarcinoma of the pancreas, or adenocarcinoma of the lung.

5 9. The method of claim 1, wherein said polypeptide is an antibody.

10 10. The method of claim 9, wherein said antibody is a monoclonal antibody.

11 11. The method of claim 9, wherein said antibody is an IgM antibody.

12. The method of claim 1, wherein said donor is a human.

13. The method of claim 1, wherein said isolated cell is a spleen cell.

15

14. The method of claim 1, wherein said isolated cell is derived from a lymph node.

15. The method of claim 1, wherein said isolated cell is derived from
20 blood.

16. The method of claim 13, 14, or 15, wherein said isolated cell is a lymphocyte.

25 17. An isolated cell expressing a polypeptide identified using the method of claim 1.

18. A purified polypeptide comprising the amino acid sequence of SEQ ID NO:1 or 3.

19. The purified polypeptide of claim 18, wherein said polypeptide comprises the amino acid sequence of SEQ ID NO:1.

20. The purified polypeptide of claim 18, wherein said polypeptide comprises the amino acid sequence of SEQ ID NO:3.

21. A purified polypeptide comprising the amino acid sequence of SEQ ID NO:5 or 7.

22. The purified polypeptide of claim 21, wherein said polypeptide comprises the amino acid sequence of SEQ ID NO:5.

23. The purified polypeptide of claim 22, wherein said polypeptide comprises the amino acid sequence of SEQ ID NO:7.

24. A purified polypeptide comprising amino acids 31-35, 50-66, and 99-107 of SEQ ID NO:1 or 23-33, 49-55, and 88-99 of SEQ ID NO:3.

25. The purified polypeptide of claim 24, wherein said polypeptide comprises amino acids 31-35, 50-66, and 99-107 of SEQ ID NO:1.

26. The purified polypeptide of claim 24, wherein said polypeptide comprises amino acids 23-33, 49-55, and 88-99 of SEQ ID NO:3.

27. A purified polypeptide comprising amino acids 31-35, 50-66, and 99-108 of SEQ ID NO:5 or 23-36, 52-58, and 91-101 of SEQ ID NO:7.

28. The purified polypeptide of claim 27, wherein said polypeptide
5 comprises amino acids 31-35, 50-66, and 99-108 of SEQ ID NO:5.

29. The purified polypeptide of claim 27, wherein said polypeptide
comprises amino acids 23-36, 52-58, and 91-101 of SEQ ID NO:7.

10 30. The purified polypeptide of any one of claims 18-29 wherein said
polypeptide is an antibody or a functional fragment thereof.

31. The purified polypeptide of claim 30, wherein said antibody is a
monoclonal antibody or a functional fragment thereof.

15

32. The purified polypeptide of claim 30, wherein said functional
fragment is selected from the group consisting of V_L , V_H , F_V , F_C , Fab, Fab', and
 $F(ab')_2$.

20 33. The purified polypeptide of claim 30, wherein said polypeptide
specifically binds to an adenocarcinoma of the colon, a diffuse-type stomach
carcinoma, an adenocarcinoma of the pancreas, and an adenocarcinoma of the
lung, and not to non-neoplastic cells of the same tissue type.

25 34. A functional fragment of an antibody, wherein said functional
fragment comprises amino acids 31-35, 50-66, and 99-107 of SEQ ID NO:1 or
23-33, 49-55, and 88-99 of SEQ ID NO:3.

35. A functional fragment of an antibody, wherein said functional fragment comprises amino acids 31-35, 50-66, and 99-108 of SEQ ID NO:5 or 23-36, 52-58, and 91-101 of SEQ ID NO:7.

5 36. The functional fragment of claim 34 or 35, wherein said functional fragment is a functional fragment of a monoclonal antibody.

37. The functional fragment of claim 34 or 35, wherein said functional fragment is a V_L chain of an antibody.

10

38. A purified polypeptide that specifically binds to a neoplastic cell, but does not bind to a non-neoplastic cell, wherein said purified polypeptide specifically binds to an adenocarcinoma of the colon, a diffuse-type stomach carcinoma, an adenocarcinoma of the pancreas, and an adenocarcinoma of the lung, and not to non-neoplastic cells of the same tissue type, and wherein said
15 purified polypeptide is substantially identical to the full-length sequence of SEQ ID NO:1 or SEQ ID NO:3.

39. The purified polypeptide of claim 38, wherein said polypeptide
20 specifically binds to at least one of EPLC-272H (DSMZ Accession Number ACC 383), Colo-699 (DSMZ Accession Number ACC 196), CACO-2 (DSMZ Accession Number ACC169, ATCC Accession Number HTB-37), Colo-206F (DSMZ Accession Number ACC 21), 23132/87 (DSMZ Accession Number ACC 201), ASPC-1 (ATCC Accession Number CRL-1682), DU-145 (DSMZ
25 Accession Number ACC 261, ATCC Accession Number HTB-81), and BM1604 (DSMZ Accession Number ACC 298) cells.

40. The purified polypeptide of claim 39, wherein said polypeptide induces apoptosis in said neoplastic cell, but does not induce apoptosis in said non-neoplastic cell.

5 41. The purified polypeptide of claim 39, wherein said polypeptide decreases proliferation of said neoplastic cell, but does not decrease proliferation of said non-neoplastic cell.

42. A purified polypeptide that specifically binds to a neoplastic cell, but
10 does not bind to a non-neoplastic cell, wherein said purified polypeptide specifically binds to an adenocarcinoma of the colon, a diffuse-type stomach carcinoma, an adenocarcinoma of the pancreas, and an adenocarcinoma of the lung, and not to non-neoplastic cells of the same tissue type, and wherein said purified polypeptide is substantially identical to the full-length sequence of SEQ
15 ID NO:5 or SEQ ID NO:7.

43. The purified polypeptide of claim 42, wherein said polypeptide specifically binds to at least one of Colo-699 (DSMZ Accession Number ACC 196), CACO-2 (DSMZ Accession Number ACC169, ATCC Accession Number
20 HTB-37), 23132/87 (DSMZ Accession Number ACC 201), DU-145 (DSMZ Accession Number ACC 261, ATCC Accession Number HTB-81), and BM1604 (DSMZ Accession Number ACC 298) cells.

44. The purified polypeptide of claim 43, wherein said polypeptide
25 induces apoptosis in said neoplastic cell, but does not induce apoptosis in said non-neoplastic cell.

45. The purified polypeptide of claim 43, wherein said polypeptide decreases proliferation of said neoplastic cell, but does not decrease proliferation of said non-neoplastic cell.

5 46. The purified polypeptide of any one of claims 18-20, 24-26, 34, and 36-41, wherein said polypeptide is also produced by the NORM-1 cell line having DSMZ deposit accession number DSM ACC2624.

10 47. The purified polypeptide of any one of claims 21-23, 27-29, 35-37, and 42-45, wherein said polypeptide is also produced by the NORM-2 cell line having DSMZ deposit accession number DSM ACC2626.

48. An isolated nucleic acid molecule comprising the sequence of SEQ ID NO:2.

15 49. An isolated nucleic acid molecule comprising the sequence of SEQ ID NO:4.

50. An isolated nucleic acid molecule comprising the sequence of SEQ ID NO:6.

20

51. An isolated nucleic acid molecule comprising the sequence of SEQ ID NO:8.

25 52. An isolated nucleic acid molecule comprising nucleic acids 91-105, 148-198, and 295-321 of SEQ ID NO:2 or 67-99, 145-165, and 262-297 of SEQ ID NO:4.

53. The isolated nucleic acid molecule of claim 52, wherein said nucleic acid molecule comprises nucleic acids 91-105, 148-198, and 295-321 of SEQ ID NO:2.

5

54. The isolated nucleic acid molecule of claim 52, wherein said nucleic acid molecule comprises nucleic acids 67-99, 145-165, and 262-297 of SEQ ID NO:4

10 55. An isolated nucleic acid molecule comprising nucleic acids 91-105, 148-198, and 295-324 of SEQ ID NO:6 or 67-108, 154-174, and 271-303 of SEQ ID NO:8.

15 56. The isolated nucleic acid molecule of claim 55, wherein said nucleic acid molecule comprises nucleic acids 91-105, 148-198, and 295-324 of SEQ ID NO:6.

20 57. The isolated nucleic acid molecule of claim 55, wherein said nucleic acid molecule comprises nucleic acids 67-108, 154-174, and 271-303 of SEQ ID NO:8.

58. A vector comprising the nucleic acid sequence of any one of claims 48-57.

25 59. An isolated cell comprising the vector of claim 58.

60. An isolated cell that expresses the polypeptide of any one of claims 18-29.

61. The isolated cell of claim 60, wherein said isolated cell is a mammalian cell.

5 62. The isolated cell of claim 61, wherein said mammalian cell is a human cell.

63. The isolated cell of claim 62, wherein said polypeptide is an antibody.

10 64. The isolated cell of claim 63, wherein said antibody is a monoclonal antibody.

65. The isolated cell of claim 63, wherein said antibody is an IgM antibody.

15 66. A method of producing the purified polypeptide of any one of claims 18-29, said method comprising contacting a cell with the vector of claim 58 and isolating the polypeptide expressed by said cell.

20 67. Use of the purified polypeptide of any one of claims 18-29 in a method of diagnosing a neoplasm in a mammal, said method comprising the steps of, (a) contacting a cell or tissue sample derived from said mammal with the purified polypeptide of any one of claims 18-29, and (b) detecting whether said purified polypeptide binds to said cell or tissue sample, wherein binding of said purified
25 polypeptide to said cell or tissue sample is indicative of said mammal having a neoplasm.

68. The use of claim 67, wherein said mammal is a human.

69. The use of claim 67, wherein said polypeptide is an antibody.

70. The use of claim 69, wherein said antibody is a monoclonal antibody.

5

71. The use of claim 67, wherein said polypeptide is conjugated to a detectable agent selected from the group consisting of a radionuclide, a fluorescent marker, an enzyme, a cytotoxin, a cytokine, and a growth inhibitor.

10

72. The use of claim 71, wherein said detectable agent is capable of inducing apoptosis of said cell.

73. The use of claim 67, wherein said polypeptide is conjugated to a protein purification tag.

15

74. The use of claim 73, wherein said protein purification tag is cleavable.

75. Use of the purified polypeptide of any one of claims 18-29 in a method of treating a proliferative disorder in a mammal, said method comprising the step of contacting a cell with the purified polypeptide of any one of claims 18-29, wherein binding of said purified polypeptide to said cell results in a reduction in proliferation of said cell.

20

76. The use of claim 75, wherein said mammal is a human.

25

77. The use of claim 75, wherein said polypeptide is an antibody.

78. The use of claim 77, wherein said antibody is a monoclonal antibody.

79. The use of claim 75, wherein said polypeptide is conjugated to a detectable agent selected from the group consisting of a radionuclide, a fluorescent marker, an enzyme, a cytotoxin, a cytokine, and a growth inhibitor.

5

80. The use of claim 79, wherein said detectable agent is capable of inhibiting cell proliferation of said cell.

81. The use of claim 75, wherein said polypeptide is conjugated to a protein purification tag.

10

82. The use of claim 81, wherein said protein purification tag is cleavable.

83. A medicament comprising the purified polypeptide of any one of claims 18-29 in a pharmaceutically acceptable carrier.

15

84. A diagnostic agent comprising the purified polypeptide of any one of claims 18-29.

85. An antibody producing cell line having DSMZ accession number DSM ACC2624.

20

86. The antibody produced by the cell line of claim 85.

87. An antibody producing cell line having DSMZ accession number DSM ACC2626.

25

88. The antibody produced by the cell line of claim 87.